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M. Dolores Sanchez de la Nieta Garcia \*, Almudena Juez del Pozo, José Antonio Cortés Toro, Antolina Rodríguez Moreno, Clara García Carro, Elena Ruiz Ferreras, Ana Isabel Sánchez Fructuoso

Hospital Clínico San Carlos, Ciudad Real, Spain

\* Corresponding author.

E-mail address: [sanchezdelanieta@senefro.org](mailto:sanchezdelanieta@senefro.org) (M.D. Sanchez de la Nieta Garcia).

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## Pseudoxanthoma elasticum and hereditary renal hypouricemia: Complication of systemic disorders or different entities? Presentation of a case

### Pseudoxantoma elasticum e hipouricemia renal hereditaria: ¿complicación de afección sistémica o entidades diferentes? Presentación de un caso



Dear Editor,

Pseudoxanthoma elasticum (PXE) is a rare genetic disorder characterised by fragmentation and calcification of elastic fibres in the skin and tunica media of arteries. Extracutaneous clinical manifestations are rare, the most common being hypertension, angina pectoris, stroke, intermittent claudication, upper gastrointestinal bleeding, angioid streaks in the retina and thickened skin.

Cases have been reported of possible association with other autoimmune diseases, such as systemic lupus erythematosus (SLE),<sup>1</sup> ankylosing spondylitis<sup>2</sup> and rheumatoid arthritis. Urologically, cases have been reported of ruptured ureters after ureteroscopy and there would seem to be a greater predisposition to urinary tract infections.<sup>3</sup>

There are no case reports linking PXE and uric acid metabolism disorders.

We present the case of a patient with PXE and hereditary renal hypouricaemia (HRH).

This was a 63-year-old woman under follow-up by Nephrology with a history of lupus nephritis class IV and mixed cryoglobulinaemia type III. No renal lithiasis. No visual problems. She first developed asymptomatic yellowish papular lesions on her neck. Suspected PXE was confirmed by skin biopsy and genetic study, by the presence of heterozygous mutation c.3662G>A (p.R1221H) in the ABCC6 gene.

In addition, analytical tests showed alterations in uric acid metabolism. The most recent test showed uricaemia 2.3 mg/dl, fractional excretion of uric acid (FEUa) 12.95%, proteinuria 0.14 g/24 h and normal urine sediment. No glycosuria or hypercalciuria. Normal acid-base balance.

After obtaining informed consent, a genetic study was requested which showed a heterozygous (+) mutation of the pathogenic variant c.1400C>T (p.T467M) in the SLC22A12 (URAT1) gene.

Reviewing the literature, this is the only report describing the presence of HRH and PXE.

PXE is known to be a multisystem disorder characterised by ectopic deposition of calcium hydroxyapatite. It is postulated that the absence of functional ABCC6 activity in the liver results in a deficiency of circulating factor(s) that are physiologically required to prevent aberrant mineralisation under normal calcium and phosphate homeostatic conditions.<sup>4</sup>

The level of hepatic expression of ABCC6 has also been shown to determine the severity of arterial calcification and infarct size after cardiac injury and is involved in the development of chronic kidney disease.<sup>5</sup>

HRH is known to be an unusual disorder characterised by a defect in uric acid reabsorption at the level of the proximal tubule. Uricaemia of less than 2 mg/dl and FEUa greater than 10% should raise suspicions.

Two types have been described: type 1 (OMIM 220150) with loss of function in the SLC22A2 gene encoding the URAT1 transporter; and renal hypouricaemia type 2 (OMIM 612076) with mutations in the SLC2A9 gene encoding the GLUT9 transporter. Homozygous forms have a more aggressive onset, with manifestations including haematuria, nephrolithiasis and renal failure after physical exercise.

It is now known to affect different ethnic groups in addition to the Asian population, in which it was originally described.<sup>6,7</sup>

The mutation in our patient diagnosed with HRH has been previously described in Roma, Spanish and Czech children and adults.<sup>8</sup>

So far no cases have been reported linking PXE and uric acid metabolism disorders, so we conclude by suggesting the importance of further study of PXE and it should be considered a paradigm in which to delve into the pathophysiology, clinical-analytical manifestations and treatment.

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Elena Borrego García<sup>a,\*</sup>, María Peña Ortega<sup>a</sup>,  
María Ramírez Gómez<sup>a</sup>, Rosa Ortega del Olmo<sup>b</sup>,  
Antonio Navas-Parejo Casado<sup>a</sup>

<sup>a</sup> Servicio de Nefrología, Hospital Universitario Clínico San Cecilio, Granada, Spain

<sup>b</sup> Departamento de Dermatología, Facultad de Medicina, Universidad de Granada, Granada, Spain

\*Corresponding author.

E-mail address: [eborregogarcia@gmail.com](mailto:eborregogarcia@gmail.com)  
(E. Borrego García).

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